REMARKS

Claim 42 has been amended to insert the wash conditions corresponding to "stringent" hybridization. It is ultimately the final wash conditions that determine stringency, so this insertion should be adequate. Support for these conditions is found on page 12, at lines 12-13. In addition, claim 42 and all pending claims have been clarified to indicate that the complement of the relevant nucleic acid is a complement over the entire length of the nucleic acid.

No new matter has been added and entry of the amendment is respectfully requested.

Rejection Under 35 U.S.C. § 112, Second Paragraph

This rejection has been addressed by amendment. Claim 42 has been amended to insert the specific wash conditions that correspond to the claim stringency. The claim dependency of claim 48 has been corrected. Accordingly, this basis for rejection is now moot.

Rejection Under 35 U.S.C. § 112, First Paragraph, Enablement

Claims 42, 45-46 and 49-51 were rejected based on insufficient information concerning the deposit referenced in these claims.

First, applicant points out that on page 69, at lines 9-13, the requested address of the depository, date of deposit and information that the deposit was under terms of the Budapest Treaty are already present in the application. Second, applicant states specifically that any and all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in the United States. This has already occurred since the grandparent has been issued. The original deposit was made before the effective filing date of the grandparent application and before the filing date of the provisional from which

the grandparent claims priority. The rejection as it pertains to the conditions of deposit is, therefore, obviated.

In another aspect of this rejection, claims 42-51 were rejected. As the Office has conceded that the application is enabling for a nucleic acid molecule that comprises a nucleotide sequence comprising the nucleotide sequence of SEQ ID NO: 1 from position 6-2138, this rejection should not apply to claim 48, which has been clarified as to its claim dependency by amendment. Applicant assumes that claim 48 as amended is free of this rejection.

In what are characterized as the second and third aspects of this rejection, the Office states that the complements of the full-length variants of SEQ ID NO: 1 from position 6-2138 are not enabled because of limited homology to the 24P4C12 mRNA, and because splice variants are putatively included.

First, because the ability to hybridize under stringent conditions is required of the variants, by virtue of the very claim language employed, it is evident that these variants would be useful in the detection of 24P4C12 mRNA. If these variants are characterized by their ability to hybridize under stringent conditions to the complement of SEQ ID NO: 1, it automatically follows that the complements of these variants would successfully hybridize to 24P4C12 mRNA "encoded" by SEQ ID NO: 1.

As to splice variants, the claims as amended for clarification do not include them. The complement is required to be over the entire length of position 6-2138, and, therefore, splice variants are irrelevant. In light of this, claim 47 should be free of the rejection for asserted lack of enablement.

The remainder of the rejection concerns the scope of claimed nucleic acid molecules defined in terms of the protein encoded and, thus, admits of degenerate coding sequences, most of which would not be useful for detection of mRNA. This aspect of the rejection is based on asserted uncertainty as to the utility of the encoded protein and, therefore, of antibodies raised against it. This assertion is evidently based on:

1. The lack of a perfect correlation between expression levels of mRNA and protein; and
2. The asserted lack of teaching of any function for the encoded protein.

Applicant recognizes that the correlation between mRNA and protein production is not perfect, but mRNA levels are not irrelevant either. Applicant is getting a little tired of this position repetitively taken by the Office. mRNA expression levels are routinely used as an index for protein production in the industry. If there were no correlation, no one would bother. mRNA expression levels are used because they are a first line of analysis providing a convenient surrogate for protein production — in order to demonstrate protein production, it would be necessary first to isolate the protein, make antibodies to it and perform analysis with these antibodies. Clearly, this is more time-consuming than simply measuring mRNA from the retrieved cDNA, and the correlation is good enough to provide useful information.

In any event, in this case, protein has been produced and antibodies to the protein have been made. Furthermore, these antibodies have been shown to be successful in inhibiting the growth of tumor cells in animal models. Enclosed herewith is the Declaration of Dr. Jean Gudas describing these results. As shown in Dr. Gudas' Declaration, in two separate animal models, monoclonal antibodies raised with respect to the 24P4C12 protein are successful in inhibiting cancer cell

growth. Accordingly, any uncertainty as to whether the levels of mRNA are indicative of protein production and any doubts as to the ability of inhibiting this protein to control cancer cell growth should be overcome. Therefore, the remaining claims, claims 42-46 and 49-51 are free of this rejection as well.

Rejection Under 35 U.S.C. § 112, First Paragraph, Written Description

Claims 42-51 were rejected on this basis citing (as usual) *Eli Lilly* and *Enzo*.

First, subparagraphs (b) and (c) in claim 42 and claims 45 and 46 clearly meet the test of *Enzo*. *Enzo* clearly held that the availability of a deposit is an adequate written description of the claimed deposited material. It may be recalled that the Court's initial finding that the deposit could not substitute for a written description was vacated and the Panel reversed itself on this point.

Second, as usual, the holding in *Lilly* has been extrapolated beyond the facts and inconsistent with the written description guidelines promulgated by the Office itself. The claims in *Lilly* were directed to a specific set of species of cDNA's which were the exact reverse transcripts of mRNA-encoding proinsulin as found in various vertebrate species. For each species there is only one answer, which answer could not be known without retrieving the reverse transcript for that specific mRNA. In contrast, the claims set forth a genus of nucleic acid molecules that are defined structurally by a required ability to hybridize to a referent substance or by a percent identity to the protein encoded. The claims are directed, therefore, to a genus of structures that is numerous, but wherein each of the structures is completely predictable by virtue of the stringency of hybridization conditions or percent identity of the encoded peptide.

Attention is called to Example 14 of the Guidelines where the claim is directed to:

> A protein having SEQ ID NO: 3 and variants thereof that are at least 95% identical to SEQ ID NO: 3 and catalyze the reaction of a → b.

In this Example, the specification only discloses SEQ ID NO: 3 but provides an assay for detecting the catalytic activity of the protein.

In the present case, the functional feature of the protein is its ability to immunoreact with antibodies raised against SEQ ID NO: 2. A high level of identity (90%) is required. Thus, the protein encoded by the nucleic acid in subparagraph (a) of claim 42 and in claim 43 meets the requirements as set forth in the Guidelines.

Similarly, the nucleic acid in paragraph (d) of claim 42 and of claim 47 meets this criterion because stringent hybridization to the disclosed sequence is required, and the utility, as recognized by the Office, resides in its ability to hybridize cross-reactively with SEQ ID NO: 1.

It should be apparent that claims 44 and 48 should not have been included in this rejection in the first place.

Rejection Under 35 U.S.C. § 102

This rejection, applied to claims 42-48, is believed obviated by the amendment to the claims which clarifies that complements must be complementary over the entire length of the disclosed sequences.

Conclusion

The claims have been amended to insert conditions of hybridization as requested by the Office and to clarify that any complementary nucleic acid molecules claimed must be complementary to the referent sequence over their entire length. These amendments obviate the rejections under 35 U.S.C. § 112, paragraph 2, and 35 U.S.C. § 102. The rejection with regard to enablement with respect to subparagraphs (b) and (c) of claim 42 and claims 45 and 46 is obviated by assuring appropriate conditions and availability of deposit. This also addresses the written

description rejection as applied to these claims. The rejection with regard to written description is inapplicable on its face to claims 44 and 48, and is misplaced with regard to the remaining claims in view of the lack of analogy of the claim language to the nature of the claim subject matter in *Lilly*. Applicant has demonstrated the utility of the encoded protein by showing efficacy of antibodies raised against it to inhibit the growth of tumors in an animal model. Accordingly, all grounds for rejection have been overcome and it is respectfully submitted that claims 42-51 are in a position for allowance.

If minor issues remain that could resolved in a telephone call, a call to the undersigned would be welcomed.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 511582001111.

Respectfully submitted,

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